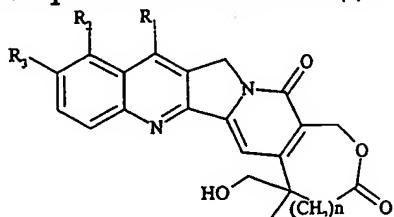
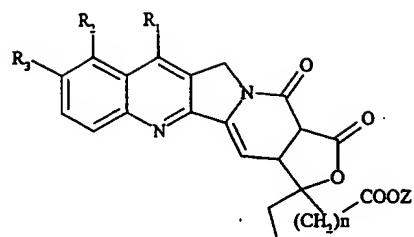


Claims

1. Compounds of formula (I) or formula (II)



(I)



(II)

where:

R_1 is hydrogen or a $-\text{C}(\text{R}_5)=\text{N}-\text{O}-\text{R}_4$ group, in which R_4 is hydrogen or a straight or branched C_1-C_5 alkyl or C_1-C_5 alkenyl group, or a C_3-C_{10} cycloalkyl group, or a straight or branched (C_3-C_{10}) cycloalkyl - (C_1-C_5) alkyl group, or a C_6-C_{14} aryl group, or a straight or branched (C_6-C_{14}) aryl - (C_1-C_5) alkyl group, or a heterocyclic group or a straight or branched heterocyclo - (C_1-C_5) alkyl group, said heterocyclic group containing at least one heteroatom selected from an atom of nitrogen, optionally substituted with an (C_1-C_5) alkyl group, and/or an atom of oxygen and/or of sulphur; said alkyl, alkenyl, cycloalkyl, cycloalkyl-alkyl, aryl, aryl-alkyl, heterocyclic or heterocyclo-alkyl groups can optionally be substituted with one or more groups selected from the group consisting of: halogen, hydroxy, C_1-C_5 alkyl, C_1-C_5 alkoxy, phenyl, cyano, nitro, and $-\text{NR}_6\text{R}_7$, where R_6 and R_7 , which may be the same or different, are hydrogen, straight or branched (C_1-C_5) alkyl, the $-\text{COOH}$ group or one of its pharmaceutically acceptable esters; or the $-\text{CONR}_8\text{R}_9$ group, where R_8 and R_9 , which may be the same or different, are hydrogen, straight or branched (C_1-C_5) alkyl; or

R_4 is a (C_6-C_{10}) aroyl or (C_6-C_{10}) arylsulphonyl residue, optionally substituted with one or more groups selected from: halogen, hydroxy, straight or branched C_1-C_5 alkyl, straight or branched C_1-C_5 alkoxy, phenyl, cyano, nitro, $-\text{NR}_{10}\text{R}_{11}$, where R_{10} and R_{11} , which may be the same or different, are hydrogen, straight or branched C_1-C_5 alkyl; or:

R_4 is a polyaminoalkyl residue; or

R₄ is a glycosyl residue;

R₅ is hydrogen, straight or branched C₁-C₅ alkyl, straight or branched C₁-C₅ alkenyl, C₃-C₁₀ cycloalkyl, straight or branched (C₃-C₁₀) cycloalkyl - (C₁-C₅) alkyl, C₆-C₁₄ aryl, straight or branched (C₆-C₁₄) aryl - (C₁-C₅) alkyl;

R₂ and R₃, which may be the same or different, are hydrogen, hydroxy, straight or branched C₁-C₅ alkoxy;

n = 1 or 2,

Z is selected from hydrogen, straight or branched C₁-C₄ alkyl;

the N₁-oxides, the racemic mixtures, their individual enantiomers, their individual diastereoisomers, their mixtures, and their pharmaceutically acceptable salts, with the proviso that, in formula (I), R₁, R₂ and R₃ cannot be simultaneously hydrogen.

2. The compounds according to claim 1, in which, in formula (I), n is 1.

3. The compounds according to claim 1, in which, in formula (II), n is 1.

4. The compounds according to claim 2, selected from the group consisting of:

- R,S-7-methoxyiminomethyl-homocamptothecin;
- R,S-7-ethoxyiminomethyl-homocamptothecin;
- R,S-7-isopropoxyiminomethyl-homocamptothecin;
- R,S-7-(2-methylbutoxy)iminomethyl-homocamptothecin;
- R,S-7-(1-t-butoxy)iminomethyl-homocamptothecin;
- R,S-7-(4-hydroxybutoxy)iminomethyl-homocamptothecin;
- R,S-7-triphenylmethoxyiminomethyl-homocamptothecin;
- R,S-7-carboxymethoxyiminomethyl-homocamptothecin;
- R,S-7-aminoethoxyiminomethyl-homocamptothecin;
- R,S-7-(N,N-dimethylaminoethoxy)iminomethyl-homocamptothecin;
- R,S-7-allyloxyiminomethyl-homocamptothecin;
- R,S-7-cyclohexyloxyiminomethyl-homocamptothecin;
- R,S-7-cyclohexylmethoxyiminomethyl-homocamptothecin;

- R,S-7-cyclooctyloxyiminomethyl-homocamptotheclin;
- R,S-7-cyclooctylmethoxyiminomethyl-homocamptotheclin;
- R,S-7-benzyloxyiminomethyl-homocamptotheclin;
- R,S-7-(benzyloxy)iminophenylmethyl-homocamptotheclin;
- R,S-7-(1-benzyloxy)iminoethyl-homocamptotheclin;
- R,S-7-(1-t-butoxy)iminoethyl-homocamptotheclin;
- R,S-7-p-nitrobenzyloxyiminomethyl-homocamptotheclin;
- R,S-7-p-methylbenzyloxyiminomethyl-homocamptotheclin;
- R,S-7-pentafluorobenzyloxyiminomethyl-homocamptotheclin;
- R,S-7-p-phenylbenzyloxyiminomethyl-homocamptotheclin;
- R,S-7-(2,4-difluorobenzylmethoxy)iminomethyl-homocamptotheclin;
- R,S-7-(4-t-butylphenylmethoxy)iminomethyl-homocamptotheclin;
- R,S-7-(1-adamantyloxy)iminomethyl-homocamptotheclin;
- R,S-7-(1-adamantylmethoxy)iminomethyl-homocamptotheclin;
- R,S-7-(2-naphthalenyloxy)iminomethyl-homocamptotheclin;
- R,S-7-(9-anthracenylmethoxy)iminomethyl-homocamptotheclin;
- R,S-7-(6-uracyl)methoxyiminomethyl-homocamptotheclin;
- R,S-7-(4-pyridil)methoxyiminomethyl-homocamptotheclin;
- R,S-7-(2-thienyl)methoxyiminomethyl-homocamptotheclin;
- R,S-7-[(N-methyl)-3-piperidinyl]methoxyiminomethyl-homocamptotheclin;
- R,S-7-hydroxyiminophenylmethyl-homocamptotheclin.

5. The compounds according to claim 3, selected from the group consisting of:

- {10-[*(E*)-(ter-butoxyimino)methyl]-3-ethyl-1,13-dioxo-11,13-dihydro-1H,3H-furo[3',4':6,7]indolizino[1,2-b]quinolin-3-yl}acetic acid
- (10-{*(E*)-[(benzyloxy)imino]methyl}-3-ethyl-1,13-dioxo-11,13-dihydro-1H,3H-furo[3',4':6,7]indolizino[1,2-b]quinolin-3-yl)acetic acid
- (3-ethyl-1,13-dioxo-11,13-dihydro-1H,3H-furo[3',4':6,7]indolizino[1,2-b]quinolin-3-yl)acetic acid
- ter-butyl ester of (3-ethyl-1,13-dioxo-11,13-dihydro-1H,3H-furo[3',4':6,7]indolizino[1,2-b]quinolin-3-yl)acetic acid.

6. Process for the preparation of formula (I) compounds according to claim 1 in which R₁ is hydrogen and R₂ and R₃ are as defined above, comprising:

- a) reduction of the keto group in position 19 of the camptothecin, optionally substituted with the envisaged meanings of R₂ and R₃, to yield the 19,20-dihydroxy-derivative;
- b) treatment of the derivative obtained in step a) with periodate and acetic acid, to obtain the opening of the E ring;
- c) Reformatsky reaction on the derivative obtained in step b);
- d) formation of the E ring where n is 1 or 2.

7. Process for the preparation of formula (I) compounds according to claim 1, in which R₁ is a $-C(R_5)=N-O-R_4$ group and R₂, R₃, R₄ and R₅ are as defined above, comprising:

- a) transformation of the camptothecin, optionally substituted with the envisaged meanings of R₂ and R₃, to 7-(dimethoxymethyl)camptothecin;
- b) reduction of the keto group in position 19 of the 7-(dimethoxymethyl)camptothecin, to yield the derivative 19,20-dihydroxy;
- c) treatment of the derivative obtained in step b) with periodate and acetic acid, to obtain the opening of the E ring;
- d) Reformatsky reaction on the derivative obtained in step c);
- e) treatment of the compound obtained in step d) with a formula R₄ONH₂ oxime and simultaneous formation of ring E where n is 1 or 2.

8. Process for the preparation of formula (II) compounds according to claim 1 in which R₁ is hydrogen and R₂ and R₃ are as defined above, comprising:

- a) reduction of the keto group in position 19 of the camptothecin, optionally substituted with the envisaged meanings of R₂ and R₃, to yield the derivative 19,20-dihydroxy;
- b) treatment of the derivative obtained in step a) with periodate and acetic acid, to obtain the opening of the E ring;
- c) Reformatsky reaction on the derivative obtained in step b);
- d) treatment of the derivative obtained in step c) with PDC with

formation of the E ring and, if so desired;

e) transformation of the Z group to hydrogen.

9. Process for the preparation of formula (II) compounds according to claim 1 in which R₁ is a -C(R₅)=N-O-R₄ group and R₂, R₃, R₄ and R₅ are as defined above, comprising:

- a) transformation of the camptothecin, optionally substituted with the envisaged meanings of R₂ and R₃, to 7-(dimethoxymethyl)camptothecin;
- b) reduction of the keto group in position 19 of the 7-(dimethoxymethyl)camptothecin, optionally substituted with the envisaged meanings of R₂ and R₃, to yield the derivative 19,20-dihydroxy;
- c) treatment of the derivative obtained in step b) with periodate and acetic acid, to obtain the opening of the E ring;
- c) Reformatsky reaction on the derivative obtained in step c);
- d) treatment of the derivative obtained in step c) with PDC with formation of the E ring;
- e) treatment of the compound obtained in step d) with an oxime of formula R₄ONH₂ and, if so desired,
- f) transformation of the Z group to hydrogen.

10. 7-(dimethoxymethyl)camptothecin.

11. Use of 7-(dimethoxymethyl)camptothecin as an intermediate product in the process according to claims 7 and 9.

12. Compounds according to any of claims 1-5 as medicaments.

13. Pharmaceutical composition containing a therapeutically effective amount of at least one compound according to claims 1-5 in admixture with pharmaceutically acceptable vehicles and excipients.

14. Pharmaceutical composition containing a therapeutically effective amount of at least one compound according to claims 1-5 in admixture

with pharmaceutically acceptable vehicles and excipients and optionally in combination with another active ingredient.

15. Pharmaceutical composition according to claim 14, in which the other active ingredient is an anticancer agent.

16. Use of a compound according to claims 1-5, for the preparation of a medicament with topoisomerase I inhibiting activity.

17. The use according to claim 16 for the preparation of a medicament useful for the treatment of tumours.

18. The use according to claim 16 for the preparation of a medicament useful for the treatment of parasitic or viral infections.